75. The method according to claim 74, wherein an overall distribution of the number of photon counts for all sections is determined through convolutions.

76. The method according to claim 73, wherein an overall distribution of the number of photon counts for a mixture of particle species is determined through convolutions.

REMARKS

Claims 29-76, presented hereby for consideration, are pending.

Present claim 29 combines subject matter from original claims 1 and 2 with subject matter found in the specification, page 5, last paragraph, the paragraph spanning pages 14 and 15, and page 15, last paragraph.

Claim 30 contains the "measurement volume" subject matter in original claim 1. Claim 1 recites "at least one measurement volume," indicating that one or more measurement volumes are studied.

Claims 31 to 34 cover subject matter disclosed on page 15, last paragraph, to page 16, first paragraph, of the specification. These claims are limited in accordance with preferred embodiments for calculating the expected distribution of the number of photon counts, which accounts for the shape of the spatial brightness function.

Claim 35 and 36 represent subject matter of claim 13. Claims 38 and 39 represent subject matter of claims 17 and 18, respectively. Claim 41 represents subject matter of claim 4, claims 42-

44 represent subject matter of claim 5, and claims 45 and 46 represent subject matter of claim 6. Claims 47-49 represent subject matter of claims 7-9, respectively. Claims 50 and 51 represent subject matter of claim 10, claims 52-55 represent subject matter of claim 11, and claims 56-59 represent subject matter of claim 12. Claims 60-66 represent subject matter of claims 14-16 and 19-24, respectively. Claims 69 and 70 represent subject matter of claim 25, and claims 71 and 72 represent subject matter of claims 26 and 27, respectively.

Concerning claims 73 to 76, the subject matter of claim 73 (which is dependent on claim 31) is found in original claim 4, and claims 74-76 are dependent, directly or indirectly, on claim 73. The subject matter of claim 74 is disclosed at the bottom of page 13 of the specification. The subject matter of claim 75 is disclosed at the top of page 14 of the specification. The subject matter of claim 76 is disclosed in the first and second paragraphs of page 14 of the specification.

Reconsideration is requested with respect to the rejection of claims under 35 USC 112, ¶2, for allegedly being indefinite. Instances of allegedly indefinite claim language are set forth in ¶s A-I in the statement of rejection.

A. The statement of rejection alleges claim 1 is indefinite due to the term"units." In accordance with the present claims, the term "units" is replaced by "particles." This amendment is supported by the specification on page 3, the last seven lines, to page 4, lines 1-5, and page 7, the last three lines, to page 8, lines 1-2.

B. The statement of rejection alleges claim 3 is indefinite due to the term "centers." The term is not found in the present claims.

C. The statement of rejection alleges claim 5 lacks antecedent basis for the term "species". By the instant amendment, claim dependency is adjusted to establish the necessary antecedent basis (cf. present claims 42 to 44).

D. The statement of rejection alleges claim 6 is indefinite due to the phrase "in particular." The phrase at issue is not found in the present claims. The feature associated with the phrase in claim 6 is made the subject matter of separate dependent claim, hereby.

E. The statement of rejection alleges claim 11 is indefinite due to the phrase "the sample is actively transported," in particular in view of the phrase "being actively transported into and out of said measurement volume." The terminology "actively transported" is not found in the present claims. (Two embodiments exemplify particle movement [transport] in and out of the measurement volume during measurement: (1) the entire particle-containing sample moves in and out of the measurement volume, e.g., the sample is put on a device, such as a Märzhauser table, which is known in the art for positioning samples in at least x- and y-directions); (2) only the particles moves in and out of the measurement volume, e.g., consider charged particles, which are transported by virtue of an electric field.)

F. The statement of rejection alleges claim 12 is indefinite due to the phrases "in particular" and "preferably". The phrases at issue are not found in the present claims. The features associated with the phrases in claim 12 are made the subject matter of separate dependent claims, hereby.

G. The statement of rejection alleges claim 13 is indefinite for use of the term "optionally." The term at issue is not recited in the present claims. The optional means for scanning and/or moving the sample are made the subject of a separate dependent claim.

H. The statement of rejection alleges claims 15-18 are indefinite because they lack antecedent basis and/or are improperly dependent. Applicant addressed this by amending the claims accordingly.

I. The statement of rejection alleges claim 20 is indefinite because it lacks antecedent basis and/or is improperly dependent. Applicant addressed this by amending the claim accordingly.

Claims 1-5, 8-14, and 19 were rejected under 35 USC 102(b) as allegedly anticipated by *Analytical Chemistry, 67*, 1995, 2849-2857 (Nie). Claims 1-6 and 8-14 were rejected under 35 USC 102(b) as allegedly anticipated by EP 601714 (Ishikawa). Reconsideration is requested with respect to the rejections.

For anticipation under § 102 to exist, each and every claim limitation, as arranged in the claim, must be found in a single prior art reference. *Jamesbury Corp. v. Litton Industrial Products, Inc.*, 225 USPQ 253 (Fed. Cir. 1985). The absence from a prior art reference of a single claim limitation negates anticipation. *Kolster Speedsteel A B v. Crucible Inc.*, 230 USPQ 81 (Fed. Cir. 1986). A reference that discloses "substantially the same invention" is not an anticipation. *Jamesbury Corp.* To anticipate the claim, each claim limitation must "*identically* appear" in the reference disclosure. *Gechter v. Davidson*, 43 USPQ2d 1030, 1032 (Fed. Cir. 1997) (*emphasis*

added). To be novelty defeating, a reference must put the public in possession of the identical invention claimed. *In re Donahue*, 226 USPQ 619 (Fed. Cir. 1985).

Applicant disagrees with the opinion of the statement of rejection that Nie anticipates the subject matter of the rejected claims. Nie does not teach or suggest the claim 1 feature of determining a distribution of the number of photon counts, neither as an experimental collection nor as a theoretical calculation. This means that Nie fails to disclose each and every limitation as arranged in the rejected claims and, therefore, the rejection under §102(b) for alleged lack of novelty based on Nie was erroneously applied against the rejected claims and, further, that the rejection cannot be applied against the present claims. *Jamesbury Corp., supra.*

Neither Ishikawa nor Nie discloses the presently claimed feature

> finding out the model of the sample yielding the closest fit between the experimentally determined and an expected distribution function of the number of photon counts, wherein the expected distribution function of the number of photon counts is calculated using characteristics of a spatial brightness function.

Without prejudice regarding the patentability of former claim 1 in view of the additional prior art cited by the statement of rejection, Evotec suggests to include into the main claim the feature of finding out the model of the sample yielding the closest fit between the experimentally determined and an expected distribution function of the number of photon counts. The expected distribution function of the number of photon counts is calculated using characteristics of a spatial brightness function.

The method according to the present invention is focused on the determination of a distribution function of specific brightness, i.e., the ability of a particle to emit radiation. The

inventors noticed that it is of importance that in a fitting process the expected function of the number of photon counts adequately accounts the spatial brightness function characteristic for the optical set-up. Especially in cases of a low specific brightness contrast of the particle species in the sample, it is of utmost importance to take the shape of the spatial brightness function of the optical set-up into account. Otherwise estimates of sample parameters would be gravely biased.

In the Applicant's view, claim 29 is new and inventive over the prior art. Neither Ishikawa nor Nie teaches or suggests finding out the model of the sample yielding the closest fit between the experimentally determined and an expected distribution function of the number of photon counts, wherein the expected distribution function of the number of photon counts is calculated using characteristics of the spatial brightness function. As discussed above, Nie not even disclose the feature of determining a distribution function of the number of photon counts.

Claim 7 was rejected under 35 USC 103(a) based on the teachings of Nie combined with the teachings U.S. Patent No. 5,763,585 (Nag). Reconsideration is requested.

According to the statement of rejection, Nie fully meets the rejected claim, except for the (6xHis) tag conjugated with the luminescently labeled Ni-NTA-derivative. Further according to the statement of rejection, Nag allegedly discloses the missing conjugate. The statement of rejection argues that it would have been obvious to use the conjugate disclosed in Nag together with the process disclosed in Nie and, thereby, arrive at the invention of claim 7. The alleged motivation for combining the separate references is "in order to be able to detect the compound at very low concentrations" (Office Action mailed December 18, 2000, page 7).

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). "All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). When conducting an obviousness analysis, "all limitations of a claim must be considered in determining the claimed subject matter as is referred to in 35 U.S.C. 103 and it is error to ignore specific limitations distinguishing over the [prior art] reference." *Ex parte Murphy*, 217 USPQ 479, 481 (PO Bd. App. 1982).

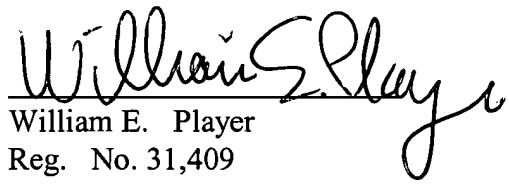
Claim 7, which is represented by claim 38 in present claims, would not have been obvious over the combined teachings of Nie and Nag for the same reasons as set forth, above, with respect to the rejection based on Nie under §102(b). Whether Nag discloses the conjugate missing from Nie, as alleged, Nag fails to cure the salient deficiency in Nie fatal to the rejection under §102(b). That is, Nie does not teach or suggest the claim feature of determining a distribution of the number of photon counts, neither as an experimental collection nor as a theoretical calculation, and Nag would have provided no motivation for one skilled in the art to modify Nie to include this claim feature. Since all limitations in claim 7 (and corresponding claim 47) are neither taught nor suggested by the cited references, a *prima facie of* obviousness has not been established. *Royka, supra*. Therefore, the §103(a) rejection of claim 7 was in error (and the rejection cannot be applied against present claim 47).

None of claims 15-18 and 20 was rejected over prior art and, consequently, the Examiner impliedly considered the corresponding subject matter free of the prior art. As such, present claims 61, 62, 38, 39, and 64, which represent subject matter of claims 15-18 and 20, respectively, are also free of the prior art, in accordance with the instant office Action.

Favorable action is requested.

Respectfully submitted,

JACOBSON·HOLMAN PLLC

By: 
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